Assessment of regulatory needs

Authority: ECHA

Group Name: silver and silver compounds

General structure: -

Revision history

Version	*Date*	*Description*
3.0	20/05/2024	

Substances within this group:

EC/List no	CAS no	Substance name [and Substance name acronyms]	Chemical structures	Registration type (full, OSII or TII, NONS, cease manufacture), highest tonnage band among all the registrations (t/y) [1]
208-047-0	506-61-6	potassium dicyanoargentate	K[Ag(CN)2]	Full, 10-100
208-048-6	506-64-9	silver cyanide	AgCN	Full, 10-100
208-590-3	534-16-7	silver carbonate	Ag2CO3	Full, not (publicly) available
219-199-2	2386-52-9	silver methanesulphonate	Ag(CH3SO3)	Full, not (publicly) available
219-641-4	2489-05-6	silver docosanoate	AgC22H43O2	Full, not (publicly) available
231-131-3	7440-22-4	silver	Ag	Full, >1000 / biocide*/ nano
231-853-9	7761-88-8	silver nitrate	AgNO3	Full, 100-1000 / Biocide*
232-033-3	7783-90-6	silver chloride	AgCl	Full, 100-1000 / Biocide*
232-038-0	7783-96-2	silver iodide	AgI	Full, 1-10
232-076-8	7785-23-1	silver bromide	AgBr	Full, not (publicly) available
233-653-7	10294-26-5	disilver(1+) sulphate	Ag2SO4	Full, 1-10
243-957-1	20667-12-3	disilver oxide	Ag2O	Full, 100-1000
416-850-4	n/a	polyphosphoric acid, copper, sodium, magnesium, calcium, silver and zinc salt	UVCB	NONS
420-090-9	n/a	GETR4	Not (publicly) available	NONS
422-570-3	n/a	silver sodium zirconium	UVCB	Full, not (publicly)

[1] The total aggregated tonnage band may be available on ECHA's webpage at https://echa.europa.eu/information-on-chemicals/registered-substances
*: under Competent Authority (Sweden) evaluation

EC/List no	CAS no	Substance name [and Substance name acronyms]	Chemical structures	Registration type (full, OSII or TII, NONS, cease manufacture), highest tonnage band among all the registrations (t/y) [1]
		hydrogen phosphate		available / biocide[2,**]
428-550-0	n/a	ARGOPHAN S	Not (publicly) available	NONS
440-610-8	n/a	SST	Not (publicly) available	NONS
460-890-5	n/a	[No public or meaningful name is available]	Not (publicly) available	NONS
603-404-0	130328-20-0	silver zinc zeolite (Zeolite, LTA framework type, surface-modified with silver and zinc ions)[3]	UVCB	No REACH registration (biocide[2,**])
620-078-5	130328-18-6	silver zeolite (Zeolite, LTA framework type, ion exchanged with silver and ammonium ions)	UVCB	No REACH registration (biocide[2,**])
n/a	130328-19-7	silver copper zeolite	UVCB	No REACH registration (biocide[2,**])
608-534-1	308069-39-8	silver phosphate glass	UVCB	No REACH registration (biocide[2,*])
n/a	n/a	silver borophosphate glass	UVCB	No REACH registration (biocide[2,*])
n/a	n/a	silver phosphoborate glass	UVCB	No REACH registration (biocide[2,*])
n/a	n/a	silver adsorbed on silicon dioxide (as a nanomaterial in	Not (publicly) available	No REACH registration (biocide[2,***] / nano)

[2] According to REACH Art. 15, active substances manufactured or imported for uses in biocidal or plant protection products only are regarded as being registered. Accordingly, although such uses are not reported in registration dossiers or there are no registrations under REACH, active substances could still be used in biocidal or plant protection products.
[3] This active substance covers the LTA (Linde Type A) framework type zeolite which has been surface-modified with both silver and zinc ions at contents Ag+ 0,5 %-6 %, Zn2 + 5 %-16 %, and potentially with phosphorus, NH4+, Mg2+ and/or Ca2+ each at level < 3 %]
**: under Commission Decision of Opinion development by Biocidal Products Committee
***: initial application for approval in progress

EC/List no	CAS no	Substance name [and Substance name acronyms]	Chemical structures	Registration type (full, OSII or TII, NONS, cease manufacture), highest tonnage band among all the registrations (t/y) [1]
		the form of a stable aggregate with primary particles in the nanoscale)		
204-786-8	126-45-4	trisilver citrate	C6H5Ag3O7	C&L notification
209-254-9	563-63-3	silver acetate	CH3COOAg	C&L notification
220-882-2	2923-28-6	silver trifluoromethane sulphonate	CAgF3O3S	C&L notification
222-006-4	3315-16-0	silver cyanate	AgOCN	C&L notification
232-035-4	7783-93-9	silver perchlorate	AgClO4	C&L notification
232-037-5	7783-95-1	silver (II) fluoride	AgF2	C&L notification
232-041-7	7783-99-5	silver nitrite	AgNO2	C&L notification
232-045-9	7784-03-4	mercury disilver tetraiodide	Ag2HgI4	C&L notification
232-048-5	7784-08-9	trisilver arsenite	Ag3AsO3	C&L notification
232-049-0	7784-09-0	trisilver orthophosphate	Ag3PO4	C&L notification
235-548-1	12271-95-3	disilver tetraborate	Ag2B4O7	C&L notification
237-956-5	14104-20-2	silver (I) tetrafluoroborate	AgBF4	C&L notification
244-438-2	21548-73-2	disilver sulphide	Ag2S	C&L notification
247-428-6	26042-63-7	silver (I) hexafluorophosphate	AgPF6	C&L notification
607-453-9	24927-67-1	silver(I)octanoate	C8H15AgO2	C&L notification
677-705-0	14242-05-8	silver perchlorate	AgClO4*H2O	C&L notification
944-224-5	n/a	reaction mass of titanium dioxide and silver chloride[2]	Not (publicly) available	C&L notification
906-230-6	n/a	silver oxylate amino complex	Not (publicly) available	Cease manufacture

The above table also contains group members that are only notified under the CLP Regulation, however, the list is not necessarily exhaustive.

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The author does not accept any liability with regard to the use that may be made of the information contained in this document. Usage of the information remains under the sole responsibility of the user. Statements made or information contained in the document are without prejudice to any further regulatory work that ECHA, the Member States or other regulatory agencies may initiate at a later stage. Assessments of regulatory needs and their conclusions are compiled on the basis of available information and may change in light of newly available information or further assessment.

Foreword

The assessment of regulatory needs of a group of substances is an iterative, informal process to help authorities consider the most appropriate way to address an identified concern for a group of substances or a single substance and decide whether further regulatory risk management activities are necessary.

The grouping is mainly based on structural similarity and associations made by the registrants between substances through read-across and category approaches as well as category associations from external sources (e.g. OECD categories)[4]. These methods are different from grouping as defined in Section 1.5 of Annex XI to REACH because the scope and intended use of ECHA's grouping is different. Thus, in this context, grouping does not aim to validate read-across and category approaches according to the Annex XI requirements but rather to support a faster and more consistent approach for regulating chemicals and avoid regrettable substitution.

The focus of the assessment is largely based on information available in the registration dossiers and on properties requiring regulatory risk management action at EU level[5]. The information reported on uses is from the registration dossiers (IUCLID) and is used as a proxy for assessing how widespread uses are and whether potential for exposure to humans and releases to the environment can be expected. The chemical safety reports are not necessarily consulted and no quantitative exposure assessment is performed at this stage.

The outcome of these assessments are proposals for immediate (the first action) and subsequent regulatory action(s), including the foreseen ultimate regulatory action (last foreseen regulatory action) to address the identified concern(s) in case the potential hazards are confirmed. For example, further data generation through compliance check is suggested as a first action, to confirm the identified hazard.

Where hazards are confirmed, regulatory risk management actions could be considered for the whole group, for a subgroup or for individual substances within the group. The robustness of the group depends on the stage of assessment and the level of certainty this stage requires. For example, the needs for grouping under restriction may differ from the needs for grouping for the purpose of harmonised classification. Group membership is reconsidered accordingly throughout the iterative assessment of regulatory needs, for example, after further information is generated and the hazard has been clarified or when new insights on uses and risks are available.

The assessment of regulatory needs in itself does not represent a regulatory action, but rather a preparatory step to consider further possible regulatory actions at the level of individual substances or groups/subgroups of substances.

[4] Working with Groups - ECHA (europa.eu)

[5] Regarding hazard properties, the focus is for instance on CMR (carcinogenic, mutagenic and/or toxic to reproduction), sensitiser, ED (endocrine disruptor), PBT/vPvB or equivalent (e.g. substances being persistent, mobile and toxic), aquatic toxicity hazard endpoints and therefore only those are reflected in the report. This does not mean that the substances do not have other known or potential hazards. In some specific cases, ECHA may consider additional hazards (e.g. neurotoxicity, STOT RE).

Publication of ARNs makes it easier for companies to follow the latest status of their substances of interest, anticipate potential regulatory actions and make strategic choices in their chemicals portfolio.

For more information on assessments of regulatory needs please consult ECHA's website[6].

[6] https://echa.europa.eu/understanding-assessment-regulatory-needs

Glossary

ARN	Assessment of Regulatory Needs
CCH	Compliance Check
CLH	Harmonised classification and labelling
CMR	Carcinogenic, mutagenic and/or toxic to reproduction
DEv	Dossier evaluation
ED	Endocrine disruptor
NONS	Notified new substances
OEL	Occupational exposure limit
OSII or TII	On-site isolated intermediate or transported isolated intermediate
PBT/vPvB	Persistent, bioaccumulative and toxic / very persistent and very bioaccumulative
PC	Product category
PMT/vPvM	Persistent, mobile, and toxic / very persistent and very mobile
RDT	Repeated dose toxicity
RMOA	Regulatory management options analysis
RRM	Regulatory risk management
SEv	Substance evaluation
STOT RE	Specific target organ toxicity, repeated exposure
STP	Sewage treatment plant
SVHC	Substance of very high concern
TPE	Testing proposal evaluation

1 Overview of the group

ECHA has grouped together 43 structurally similar silver compounds based on the presence of silver in the structure (Ag, Ag^+). The group consists of different types of compounds with Ag (primarily as Ag^+), including both simple and more complex substances, e.g. compounds with different inorganic or organic counter ion(s), various levels of complexity and forms (e.g. nanoparticles, NP). Elemental silver (Ag metal) is also included in the group.

There are 13 silver-containing compounds with full REACH registrations, four of which are also biocidal active substances in the meaning of Regulation (EU) No 528/2012 (hereafter 'BPR'). Seven group members have uses only under the BPR. There are five notified new substances (NONS) of which one is claimed under REACH, four are unclaimed (now revoked) and 17 are non-registered substances with C&L notifications only. For one REACH registered substance, there has been a cease of manufacture. The REACH registration of silver encompasses elemental, massive and nanoforms of silver.

Based on information reported in the REACH registration dossiers, the use description under REACH for many of the registered substances in the group is generic, also for the substances registered in the higher tonnage bands i.e. >100 tons per year (t/y). Uses of these silver compounds are predominately industrial, but there are some notable professional and consumer uses that could lead to exposures, particularly for silver (e.g. in the production of jewellery) and silver halides (i.e. in 'wet' photographic processes). Uses of silver compounds in textiles (substance in article), which could also be reasonably considered to result in releases to the environment, are not reported in the REACH registration dossiers, but the use of various silver substances in textiles as a biocide have been applied for and are currently under review. For nanosilver, consumer exposure depends on the location of the nanomaterial in consumer/medical products and/or the manipulation of the product. To determine the level of exposure, more information is needed on the concentrations of silver in products, the size and the form in which it is present and the probability of release of Ag-NP or Ag ions from the products.

Silver metal and silver nitrate have the most diverse use profiles. Silver metal (registered >1 000 t/y) has widespread uses with a use profile comprising of a number of industrial, professional, consumer or article service life exposure scenarios. The majority of uses of silver metal are industrial (e.g. uses related to electronics, semi-conductors, photo-voltaic applications and batteries, surface treatment (PC14) and the formulation of and industrial use of conductive adhesives, silicones and paints), in addition silver metal and silver-containing alloys are used in the production of articles. Silver is also used as a food contact material and as a food additive (E174) but these uses are assessed by EFSA under separate legislations. Silver metal is potentially of greatest concern from the perspective of exposure, in particular of industrial and professional workers.

Silver nitrate (registered 100-1000 t/y) has limited widespread uses, specifically uses associated with photography (professional and article service life) and as laboratory chemicals (professional only). Silver carbonate (EC 208-590-3) is used as an intermediate in the production of other silver compounds. Previously it was also registered for consumer use in pharmaceuticals as 'an active ingredient in antibiotic cream'.

Uses of silver compounds as biocidal active substances are extremely diverse in products and articles. Silver metal (EC 231-131-3) is also a biocidal active

substance and was thus subject to harmonised classification and labelling (CLH)[7] in line with Article 36 of Regulation 1272/2008 (hereafter 'CLP'). The CLH proposal of silver resulted in three separate entries (massive [≥ 1 mm], powder [> 100 nm < 1 mm] and nano [> 1 nm ≤ 100 nm]) due to differences in aquatic toxicity between massive, particle and nanoforms. The biocidal active substance silver zinc zeolite (EC 603-404-0) has a CLH as Repr. 2, H361d (for development).

The BPR substances are at different stages of evaluation and approval. The evaluation of silver sodium hydrogen zirconium phosphate, silver zeolite and silver copper zeolite for product types 2 (disinfectants for not direct use in humans and animals) and 7 (film preservatives) has been finalised leading to a non-approval decision for all. However, the reason for the non-approval decisions was the efficacy which could not be sufficiently demonstrated.

For product type 4 (food and feed disinfectants) uses in food contact material and preservation of water filters, coordination with EFSA has taken place to ensure consistency in the risk assessment methodologies[8]. The Biocidal Product Committee proposed in March 2021 the non-approval of silver sodium hydrogen zirconium phosphate, silver zeolite, silver copper zeolite and silver zinc zeolite due to unacceptable risk identified for consumers exposed to silver compounds via the diet, from food contact materials and water filters. The consumption of filtered water showed acceptable risk for adults, children and toddlers, but not for infants. The non approval proposals for silver copper zeolite and silver sodium hydrogen zirconium phosphate were also based on lack of sufficiently demonstrated efficacy. In September 2023, the Standing Committee for Biocides decided the non-approval of silver sodium hydrogen zirconium phosphate, silver zeolite, silver copper zeolite and silver zinc zeolite.

Thus, from all the above substances, only silver zinc zeolite is approved for product types 2, 7 and 9 (fibre, leather, rubber and polymerised materials, preservatives). The rest of the silver substances notified under BPR are under evaluation by the Swedish evaluating Competent Authority (SE eCA). In addition, the pesticidal active substance silver thiosulfate complex has been approved under Plant Protection Product Regulation 1107/2009 as a plant growth regulator on cut flowers.

[7] Classified as Repr. 2 (for fertility), STOT RE 2 (nervous system) and for powder and nanoforms, as Aquatic Acute 1 and Chronic 1. See link at https://echa.europa.eu/documents/10162/5b4397d9-7339-251a-98e6-c67774664204

[8] https://www.efsa.europa.eu/sites/default/files/2021-02/joint-efsa-echa-comparison-evaluations-perfomed-silver-compounds-biocidal-active-substances-fcm.pdf

2 Conclusions and proposed actions

The conclusions and actions proposed in the table 1 below are based mainly on the REACH and CLP information available at the time of the assessment by ECHA. Information sources included Competent Authority Reports under the biocidal regulation (CARs), Harmonised Classification and Labelling (CLH) documents including opinions from the Risk Assessment Committee (RAC), literature data as well as REACH dossiers with Chemical Safety Reports (CSR). The CLH proposal of silver resulted in three separate entries (massive [≥ 1 mm], powder [> 100 nm < 1 mm] and nano [> 1 nm ≤ 100 nm]) due to differences in aquatic toxicity between massive, particle and nanoforms.

Some concerns for human health have recently been clarified or confirmed by the results of an extended one-generation reproductive toxicity (EOGRT) study (with silver acetate), new *in vivo* toxicokinetics data (various silver forms), literature data included in the RAC opinion for silver and an *in vivo* genotoxicity study with potassium dicyanoargentate (EC 208-047-0). Further, silver nanoparticles and several silver substances have been self-classified by registrants as Repr. 1B (H360D). In addition, for non-CMR human health hazards, there was a screening by ECHA of information only in the REACH dossiers.

Overall, available test data for individual substances is rather low and read-across is applied by registrants for many substances to silver metal (and other compounds) to fulfil information requirements. The conclusions are preliminary suggestions from a screening-level assessment done by ECHA with the aim to propose the next steps for further work (e.g., strengthening of the hazard conclusions, clarification of the uses and/or potential for exposure). When new information (e.g., on hazards through evaluation processes, or on uses) will become available, the document may be updated, and conclusions and actions revisited.

Table 1: Conclusions and proposed actions

Subgroup name, EC/List no, substance name	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Suggested regulatory actions
EC 231-131-3 (Silver (metal) massive [≥ 1 mm], powder [> 100 nm < 1 mm] and nano [> 1 nm ≤ 100 nm])	Known or potential hazard for reproductive toxicity for all (Silver nitrate, disilver(I) sulphate,	Known or potential hazard for aquatic toxicity	Widespread and high tonnage industrial, professional and consumer uses with high environmental and human exposure potential.	**First step:** CCH for silver metal, silver carbonate, all subgroup 2 silver compounds **Potential next steps (if hazard confirmed after data generation):**

Subgroup name, EC/List no, substance name	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Suggested regulatory actions
EC 208-590-3 (Silver carbonate) **Subgroup 1 (Highly soluble compounds)** EC 231-853-9 (Silver nitrate) EC 209-254-9 (Silver acetate) (not registered) EC 219-199-2 (Silver methane sulphonate) EC 233-653-7 (disilver(I) sulphate) **Subgroup 2 (low solubility compounds)** EC 243-957-1 (disilver oxide) EC 232-076-8 (silver bromide)	Silver nanoform, silver carbonate and all subgroup 2 substances self-classified as Repr. 1B (H360D), silver metal CLH as Repr 2) for STOT RE for all for ED for silver bromide and iodide due to the counter ions Inconclusive hazard for carcinogenicity for mutagenicity for skin sensitisation (all but silver metal) for ED (for all but the two identified above)		Biocidal uses for silver nitrate, silver chloride, Silver methane sulphonate with industrial uses only Nanoform of silver chloride cannot be excluded.	CLH for repro 1B (group approach for at least soluble silver compounds to be explored) (CLH already ongoing for silver nitrate based on data on silver acetate) **Potential last action:** **EU wide exposure limit for workers** by setting either an OEL under the Chemical Agents Directive (Directive 98/24/EC) or by a restriction under REACH. <u>Justification</u>: Harmonised classification as Repr 1 would lead to generic restriction of the substance(s) in consumer mixtures by means of restriction entry 30. Self-classification may also not be sufficient to ensure safe use for human health or the environment as many notifiers do not self-classify the substances. CLH will also support regulatory action under other regulations including

Subgroup name, EC/List no, substance name	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Suggested regulatory actions
EC 232-033-3 (silver chloride) EC 232-038-0 (silver iodide)				derivation of an EU-wide exposure limit for workers under OSH or REACH restriction.
EC 208-047-0 (potassium dicyanoargentate)	Known or potential hazard for ED For reproductive toxicity STOT RE Inconclusive hazard for carcinogenicity for skin sensitisation for mutagenicity		Professional: Metal and non-metal surface treatment products. Cyanide release is expected during uses.	**First steps:** Pending Action (assessment of study following TPE for in vivo mutagenicity). Substance evaluation to investigate ED concerns observed in the OECD TG 422 study (thyroid modality). **Potential next steps (if hazard confirmed after data generation):** SVHC identification/CLH **Potential last action:** **Restriction** <u>Justification</u>: The reported professional uses are widespread (at many sites and many users) with relatively low levels of operational controls and risk management measures but with often frequent exposures with a long

Subgroup name, EC/List no, substance name	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Suggested regulatory actions
				duration. Restriction of professional uses is preferred over authorisation as it is considered to be more efficient and effective to introduce controls at the level of placing on the market rather than at the level of uses. Potential exposure from articles needs further investigation, restriction for use in articles to be considered together with the restriction of professional uses.
EC 219-641-4 (Silver docosanoate)	Inconclusive hazard for reproductive toxicity for carcinogenicity for mutagenicity for STOT RE for skin sensitisation for ED		Industrial uses only	**First step:** CCH **Potential last action:** **Currently not possible to assess the regulatory needs** <u>Justification</u>: The information on hazard is not sufficient to conclude on the needs for regulatory risk management actions. This will be reassessed once generation of data is completed (CCH).
EC 208-048-6 (Silver	Inconclusive hazard		Professional	No action

Subgroup name, EC/List no, substance name	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Suggested regulatory actions
cyanide)	for carcinogenicity for ED		Metal surface treatment products. Cyanide release is expected during uses.	**Currently not possible to assess the regulatory needs** Justification: Actions (including data generation) will be re-considered when the assessment will be revisited if the registration status changes. Self or harmonised classification for human health and aquatic toxicity followed by implementation of necessary RRMs should be sufficient to ensure safe use.
EC 422-570-3 (Silver sodium zirconium hydrogenphosphate)	Inconclusive hazard for carcinogenicity for ED for STOT RE		Former NONS Biocidal uses (Silver (ion) release expected)	No action **Potential last action:** **Currently not possible to assess the regulatory needs** Justification: Harmonised classification ongoing for aquatic toxicity. Self or harmonised classification for human health and aquatic toxicity

Subgroup name, EC/List no, substance name	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Suggested regulatory actions
				followed by implementation of necessary RRMs should be sufficient to ensure safe use Biocidal uses to be addressed under the BPR.
Five NONs substances (one claimed and four unclaimed, now revoked)	Inconclusive hazard for carcinogenicity for ED for STOT RE for reproductive toxicity for mutagenicity for skin sensitisation		Claimed or unclaimed NONS without tonnage upgrades, mainly industrial uses.	No action **Currently no need for EU RRM** Due to the substances being NONs no data generation is possible to clarify the hazards currently. Actions (including data generation) will be re-considered when the assessment will be revisited if the registration status and/or uses change.
Eight substances with only biocidal uses			Not registered under REACH. Potential for exposure for professional workers and release to the environment cannot be excluded.	No action **Currently no need for EU RRM** Due to the substances not being registered under REACH no data generation is possible to clarify the hazards currently. Actions (including data generation) will be re-considered when the assessment will be revisited

Subgroup name, EC/List no, substance name	Human Health Hazard	Environmental Hazard	Relevant use(s) & exposure potential	Suggested regulatory actions
				if the registration status and/or uses change. Biocidal uses to be addressed under the BPR.

3 Justification for the need for regulatory risk management action at EU level (if hazards confirmed)

In previous ECHA regulatory processes, silver metal (EC 231-131-3) has been examined under substance evaluation (SEv, 2014) and under CLP by RAC (ECHA, 2022) with a CLH dossier submitted by the Swedish Competent Authority. The SEv was restricted to the assessment of environmental concerns related to nanoforms of silver and concluded that ionic silver is either equally or more toxic than nanoforms of silver. Following the RAC opinion on silver metal, the CLH proposal of silver resulted in three separate entries (massive [≥ 1 mm], powder [> 100 nm < 1 mm] and nano [> 1 nm ≤ 100 nm]) due to differences in aquatic toxicity between massive, particle and nanoforms. RAC concluded that a generic read-across approach with a basic assumption that the systemic toxicity of any of the inorganic silver compounds is driven by the silver ion (Ag+) cannot be pursued. RAC pointed out the uncertainties regarding several human health hazard endpoints for silver (e.g. mutagenicity) and did not support the read-across strategy proposed by the CLH Dossier Submitter.

The silver ion, Ag+, is recognised as the toxicophore, but it is necessary to consider the potential toxicity of silver metal in reduced and aggregated form such as nanoparticles or massive forms compared to that from exposure to silver salts, such as silver nitrate (AgNO3), ion exchange matrices such as silver zeolites or other elements such as zinc or copper which may contribute to toxicity. In addition to the toxic potential of the silver ion, particle-related effects such as (local) inflammatory (foreign body) responses, adsorption, persistence, carry-over effects, translocation, and cellular uptake have to be considered. Therefore, silver (metal) and other silver compounds have not been grouped into a large group in the ARN for the purpose of human health hazard assessment and regulatory action.

Suggested regulatory risk management action for silver metal, all subgroup 1 and 2 substances and silver carbonate (EC 208-590-3) if reproductive toxicity hazard is confirmed. Furthermore, for two subgroup 2 substances **silver bromide (EC 232-076-8) and silver iodide (EC 232-038-0)** as well as for **potassium dicyanoargentate (EC 208-047-0)** regulatory risk management action needs to also consider **ED hazard** (for human health and non-target organisms) if the hazard is confirmed. For the latter substance, the ED concern (thyroid) is based on the results from a recent OECD TG 422 study. For silver bromide and iodide, the concern is related to the toxicity of the counter-ions to the thyroid.

Based on currently available information, there is a potential hazard for reproductive toxicity due to the potential for release/exposure from industrial, professional, consumer and article uses of silver metal (all forms), soluble silver compounds (subgroup 1; EC 231-853-9 silver nitrate, EC 209-254-9 silver acetate (not registered), EC 219-199-2 silver methane sulphonate and EC 233-653-7 disilver(I) sulphate) and low solubility silver compounds (subgroup 2) (EC 243-957-1 disilver oxide, EC 232-076-8 silver bromide, EC 232-033-3 silver chloride and EC 232-038-0 silver iodide). In addition, EC 208-590-3 silver carbonate, used as an intermediate in production of other silver compounds and

previously registered for consumer use in pharmaceuticals as 'an active ingredient in antibiotic cream', has the same potential reproductive toxicity hazard.

In 2022 RAC assessed the need for CLH of silver metal (EC 231-131-3; massive, powder and nanoform; ECHA, 2022). As already briefly indicated above, the RAC concluded that a generic read-across approach with a basic assumption that the systemic toxicity of any of the inorganic silver compounds is driven by the silver ion (Ag+) cannot be pursued, due to different bioavailability considerations. According to RAC, the clear developmental effects observed by silver acetate are not at this moment in time considered representative of silver metal via read-across. In the absence of well conducted, guideline and GLP-compliant silver nanoparticle investigations into developmental effects, RAC considered there was insufficient data for an assessment of silver developmental toxicity and therefore did not propose classification for development for silver.

For effects on sexual function and fertility, according to RAC, the public literature supported the classification of all silver forms as Repr. 2 (H361f) but "*because of limitations in the various studies […] a case for category 1 classification of silver is not sufficiently robust*" (ECHA, 2022). RAC also concluded that "*a great deal of uncertainty remains regarding the overall robustness of data for adverse effects"*. This concerned data on silver in nanoform. The available data on silver acetate were considered as clear developmental effects.

For developmental toxicity, similarly to fertility endpoints, the results of the EOGRTS with silver acetate (EC 209-254-9) were not used by RAC as it "*represents the worst-case scenario with respect to the greatest bioavailability of Ag+ ions" and "the bioavailability of Ag+ ions from a soluble silver salt is not representative of the bioavailability of Ag+ ions from silver metal*". RAC further concluded that "*in the absence of well conducted, guideline and GLP-compliant silver nanoparticle investigations into developmental effects, […] there is insufficient data for an assessment of silver developmental toxicity and therefore, does not propose classification for development for silver*".

On the contrary, the registrants have considered, using weight of evidence, that the data show different effects between silver metal (massive and powder) and nanosilver based on bioavailability considerations and a copper-depletion and deficiency mode of action. Consequently, in the registration dossier of silver metal a more stringent classification of Repr. 1B (H360D) has been applied for nano silver on the basis of the EOGRTS study on silver acetate. According to the C&L inventory, the new self-classification as Repr. 1B are not applied by notifiers. Normally, where the notification results in different classifications on the inventory for the same substance, the notifiers and registrants shall make every effort to come to an agreed entry to be included in the inventory (CLP Regulation, Article 40). Experience has shown that divergences in self-classifications for substances with no CLH are not clarified by registrants.

Overall, there is a remaining uncertainty for reproductive toxicity of silver metal, in particular for the nano form. The updated information in the registration dossier, including the read-across approaches used, need to be assessed via a compliance check (CCH) according to the data requirements given in the relevant regulatory framework (BPR and REACH). The CCH should also consider the availability of information requirements according to the revised REACH Annexes for nanoforms of substances by 1 January 2020, to consider the self-classification of nanosilver as Repr. 1B (H360D) and its limited industrial uses (sintering as a conductive in electronics). If considered necessary a EOGRTS with DNT cohort with nanosilver may be requested.

The low solubility silver compounds (subgroup 2) are all self-classified as Repr. 1B (H360D; based on data on soluble silver compounds). There is a potential hazard for reproductive toxicity, however for these low solubility silver compounds CCH is proposed as first step to ensure compliance with REACH data requirements and to investigate the hazards.

The first step of the regulatory risk management, should the reproductive toxicity hazard exist, is the confirmation of hazard via harmonised classification (CLH) as reproductive toxicity hazard for the substances identified above. When preparing the CLH proposals, it may be considered what would be the best way to develop them, for instance whether to make a proposal for the group of substances, to submit them individually or jointly.

Silver nitrate (EC 231-853-9; a biocidal active substance) is currently under CLH with a proposal for Repr. 1B (H360FD; the RAC opinion should be available in 2024[9]). The CLH proposal is largely based on data from other soluble silver compounds, including silver acetate (developmental (neuro)toxicity including necrosis in the brain and changes in neurobehavioural parameters in the EOGRT study). The results are proposed to confirm the developmental toxicity hazard. It is suggested to group in an Annex VI entry, silver acetate with other highly soluble silver compounds (subgroup 1).

If the CLH process confirms the substances as being Repro cat. 1B then the CLH will require company level risk management measures (RMM) for workers to be in place. In particular, if the (neuro)developmental hazard properties have been confirmed during the CLH process, there is a need for additional protection of sensitive (worker and professional) populations, including pregnant women, breastfeeding women and young people at work. The CLH as Repr. 1B, H360D would protect these sensitive populations at work (1994/33/EC and 92/85/EC) provided that the employer concludes that there is also harmful exposure/identified risk in the work (i.e. the hazard per se is not sufficient for implementing protective measures). There are also generic consequences for workers applicable to all hazardous substances (98/24/EC).

In addition, CLH is needed or highly recommended in support of further regulatory processes under REACH; and it would lead to generic restriction of the substance(s) in consumer mixtures by means of restriction entry 30.

CLH is also a prerequisite to restrict the presence of the substances in clothing, other textiles, and footwear articles, by means of the restriction entry 72 of REACH Annex XVII. This would however require the addition of the relevant substances to Appendix 12 by the Commission through Article 68(2). Based on the information available, only nanosilver has uses in textiles.

CLH will also support regulatory action under other legislations. For instance, in this specific case

- harmonised classification as CMR cat. 1 will trigger regulatory action under the Cosmetic products regulation (EC) No 1223/2009, since CMR cat. 1 are restricted by this regulation unless specifically derogated. This may be relevant for silver carbonate (EC 208-590-3) which was previously registered for consumer use as "an active ingredient in antibiotic cream" (PC 29: pharmaceuticals).

[9] Harmonised classification and labelling consultations - ECHA (europa.eu)

- harmonised classification as CMR cat. 1 would render the substances unacceptable as co-formulants in biocidal products if present above the concentration limit leading to classification of the mixture as CMR cat 1 according to the Biocidal product regulation (EU) 528/2012.
- harmonised classification as CMR cat. 1 would render the substances unacceptable co-formulants in Plant Protection Products if present above the concentration limit leading to classification of the mixture as CMR cat 1 according to the plant protection product regulation (EC) No 1107/2009.
- harmonised classification as CMR cat.1 will trigger the restriction of use of these substances in toys according to the Toy Safety Directive (2009/48/EC).

As introduced above, biocidal active substances meeting the exclusion criteria will in principle not be approved for use. This includes substances classified as carcinogens, mutagens and reprotoxic substances categories 1A or 1B according to the CLP Regulation or substances identified as endocrine disruptors. Biocidal compounds may also be excluded if they are inserted in CLP as a group entry for the same hazard. According to the BPR, derogations are foreseen, in particular when the active substance may be needed on the grounds of public health or of public interest when no alternatives are available. In this case, provided that other unacceptable risks are identified, approval of silver and silver compounds could be granted for a maximum of five years. Of the substances proposed for CLH based on reproductive toxicity (if hazards confirmed) silver, silver chloride and silver nitrate are also biocidal active substances.

Following the CLH, or alongside it, the next step of the regulatory risk management proposed is the setting up of an **EU-wide exposure limit for workers** which can be implemented either by setting a binding occupation exposure limit (OEL) under the Chemical Agents Directive (Directive 98/24/EC) or by a restriction under REACH due to potential for exposure of professional and industrial users of soluble silver compounds (subgroup 1), low solubility silver compounds (subgroup 2), silver carbonate and metallic silver forms.

For nanosilver, the development of an OEL under Directive 2004/37/EC (CMDR) could be initiated after the CLH process and the generation of data under REACH which may confirm additional hazards e.g. mutagenicity. Or alternatively, it could already be initiated on the basis of the self-classification of nanosilver as Repr. 1B (H360D) and repeated dose toxicity effects which cannot be ruled out in workers (SCENIHR, 2014; Drake and Hazelwood, 2005; Weldon *et al.*, 2016). The increased number of applications of silver nanoparticles and their integration into consumer and professional products can be expected to impact the exposure of workers to silver nanoparticles during manufacturing, handling, and disposal.

There may also be a need to update the existing exposure limits for metallic silver (currently 0.1 mg/m3 as total dusts (SCOEL, 1993) and IOELV for soluble silver compounds (2006/15/EC)). Existing OELs and IOELV are based on (local) argyria (pigmentation or staining of the tissues). These are irreversible effects that are not considered to damage health. The American Conference of Governmental Industrial Hygienists (ACGIH, 2011) confirmed that exposure limits of 0.01 mg/m^3 for soluble silver and 0.1 mg/ m^3 for metallic silver were adequate to prevent argyria and other skin damage in workers exposed to airborne silver. Some of these OELs are in place at national level in the EU (Directive 2006/15/EC; GESTIS International Limit Values (dguv.de)). For metallic silver, inconclusive hazards (carcinogenicity, mutagenicity, developmental toxicity) will need to be clarified.

For specific biocidal substances, the acceptable exposure limits (AELs) for professionals and/or operators derived under Biocidal Products Regulation or Plant Protection Products Regulation appear significantly lower than the current OELs (see above). EFSA derived an ADI of 0.3 µg/kg bw/d for silver (E 174) based on silver ions (EFSA, 2021).

Overall, OELs would trigger the need for additional worker's protection and risk assessment that usually includes an estimation of exposure. Depending on the type of OEL and the implementation on each MS, OELs may trigger an obligation to monitor workplace exposure (e.g. often the case for CMRs). Thus, normally when an OEL is established, air monitoring methods (and biomonitoring methods in the cases of BLVs) need to be developed. Feasibility monitoring the proposed OELs according to OSH standards (e.g. EN 482) is considered when proposing or implementing the OEL. If an EU binding limit value is set for silver compounds, Member States must establish national exposure limit values. National OELs cannot be higher that the EU binding OEL (it is a ceiling) but may be more stringent. Additionally, biological Limit Values (BLVs) are currently set in accordance with the CAD. They constitute limits of the concentration in the appropriate biological medium (e.g. blood, urine) of the relevant agent, its metabolite, or an indicator of effect.

Based on currently available information, there is also a **potential hazard for STOT RE** for the soluble silver compounds (subgroup 1) as, in addition to reproductive toxicity, the most concerning hazard effect noted by RAC is (developmental) neurotoxicity of silver and consequently RAC classified silver metal (all forms) as STOT RE 2 (nervous system). According to RAC, "*Taking a weight of evidence approach which included a selection of different studies, mainly with silver NPs, which consistently show morphological and/or functional neurotoxic effects, it was concluded that classification for STOT RE was warranted. While some neurotoxic effects occurred within the guidance value range for STOT RE 1, that category was not proposed by RAC because the overall database on the lowest dose levels where hippocampus toxicity and neurofunctional deficits involving learning and memory started to occur was considered insufficiently robust or inconsistent to support the more severe category*" (ECHA, 2022).

The nervous system was identified as the target organ for the soluble forms of silver based on the recent EOGRT study with silver acetate (EC 209-254-9; Anon., 2021, Anon., 2022). These results raise neurotoxicity concern for also the other soluble silver compounds (subgroup 1) after repeated dose toxicity (RDT). However, STOT RE is a potency-dependent hazard class. Therefore, it may be difficult to justify a group CLH classification via read-across between substances for which the potency differences cannot be estimated due to differences in bioavailability. It is also uncertain if the neurotoxic effects seen after silver nanoparticle exposure are nanoparticle effects or (silver) ionic effects or a combination of both. Following the argumentation in the RAC opinion on silver, read-across from silver nanoparticles to other silver compounds may be difficult to justify. For soluble silver compounds (subgroup 1) proposed for CLH as Repr. 1B as well as other silver compounds self-classified as Repr. 1B (H360D; subgroup 2 and silver carbonate), an additional STOT RE classification may not bring further risk management measures. No further regulatory action is therefore proposed to address the potential STOT RE hazard of these silver compounds. Nevertheless, during the CLH process for reproductive toxicity a dossier submitter may also consider the possibility of including the STOT RE hazard in the proposal.

Regarding endocrine disruption (ED), based on currently available information, silver bromide (EC 232-076-8) and silver iodide (EC 232-038-0) as well as potassium dicyanoargentate (EC 208-047-0) have a **potential hazard for ED** for human health and non-target organisms.

The potential hazard for endocrine disruption (ED) for human health and non-target organisms is known for substances containing and releasing bromide and iodide, like silver bromide (EC 232-076-8) and silver iodide (EC 232-038-0). There are indications from other bromide substances (e.g., 2,2-dibromo-2-cyanoacetamide, DBNPA, EC 233-539-7) that this counter-ion has the potential for displacing iodine in the thyroid and cause endocrine (thyroid) effects that might be relevant for humans[10]. In addition, the thyroid function depends on iodine uptake[11]. Therefore, silver bromide (EC 232-076-8) and silver iodide (EC 232-038-0) are considered ED by default. There is currently no need to generate further data to clarify the concern for endocrine disruption and there is sufficient information to support this conclusion. However, a number of uncertainties regarding the setting of a threshold for these ED properties as well as the natural occurrence and essentiality of bromide and iodide should be considered. Further work might be needed to examine overall contribution of exposure to bromide and iodide from various sources/releases and a potential need for risk management for the endocrine disruptive properties for human health and environment[12]. The regulatory risk management action already proposed for these two halide- containing substances will limit the exposure to these substances.

For potassium dicyanoargentate (EC 208-047-0), thyroid toxicity has been observed in the recent OECD TG 422 study. Effects on the thyroid included increased incidences of minimal follicular cell hypertrophy at all dose levels (1, 3 and 10 mg/kg bw/day) in males and females. Registrants considered these effects as an exacerbation of a spontaneous finding and as non-adverse, which is unlikely. Therefore, data generation is proposed via SEv to further investigate the potential for thyroid disruption for human health in line with the EFSA/ECHA ED Guidance, 2018 (Appendix A: Additional considerations on how to assess the potential).

Following the SEv, the first step of the regulatory risk management action proposed, should the hazard be confirmed, is to propose SVHC identification under REACH/CLH under CLP[13]. SVHC identification is highly recommended as a step prior to restriction. In addition, SVHC identification brings immediate obligations for suppliers of the substances such as (i) supplying a safety data sheet and communicating on the safe use of the substances, (ii) responding to

[10] Biocidal Products Committee (BPC). Opinion on the application for approval of the active substance: 2,2-Dibromo-2-cyanoacetamide (DBNPA). Product type: 4. ECHA/BPC/300/2021. Available at https://echa.europa.eu/documents/10162/085a4896-b067-bdbc-e38c-8f794e60e4f3

[11] EFSA/ECHA Guidance for the identification of endocrine disruptors in the context of Regulations (EU) No 528/2012 and (EC)No 1107/2009. 2018. Available at https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2018.5311

[12] https://echa.europa.eu/documents/10162/c984aeda-ac67-8be2-57f3-43c797cf293d

[13] The hazard classes PBT/vPvB, PMT/vPvM, ED have been introduced in CLP: CLP Delegated Act (europa.eu). Therefore, instead of SVHC identification under REACH, these hazards may be confirmed via CLH. It is not clear when to use which legal route (SVHC under REACH or CLH under CLP) during the period that both legal options are available.

consumer requests within 45 days and (iii) notifying ECHA if the article they produce contains the substance above regulatory threshold.

Potassium dicyanoargentate is used by industrial and professional workers in electroplating and metal surface treatment in settings where there is opportunity for exposure (e.g. PROC 4: chemical production where opportunity for exposure arises, PROC 13: treatment of articles by dipping and pouring). The professional uses of metal surface treatment products are expected to be widespread (at many sites and by many users). Professional use is often widespread with relatively low levels of operational controls and risk management measures but with often frequent exposures with a long duration. In addition, professional users may be self-employed and therefore not covered by occupational safety and health (OSH) legislation.

Therefore, a **restriction of the substance as such or in mixtures (concentration limit in mixtures) used by professionals** is suggested after CLH.

Restriction of professional uses is preferred over authorisation as it is considered to be more efficient and effective to introduce controls at the level of placing on the market rather than at the level of uses. In addition, the use of the most harmful substances by professional workers has been recognised as an area of concern under the European Commission's Chemicals Strategy for Sustainability[14] which aims to extend to professional users under REACH the level of protection granted to consumers.

Moreover, potential exposure from articles needs further investigation. The need for restricting substances in articles used by professionals or consumers (based on information on ECHA website there is article use by consumers) should be considered in the context of the restriction of professional uses.

Based on currently available information, **there is a potential hazard for aquatic toxicity hazards for all silver compounds**, however there is **no need for further regulatory risk management** action on this aspect as explained below.

Aquatic toxicity hazards have been identified for all members of the group. Here, classification as Aquatic Acute 1 and Aquatic Chronic 1 apply to each substance with some variations in the applicable M-factors. In all cases, it appears that silver and its compounds are considered as not rapidly transformed to non-bioavailable forms and it is difficult to reach a conclusion regarding bioaccumulation, although the evidence appears to lean towards it not being bioaccumulative in organisms.

As silver nitrate (EC 231-853-9) is currently in the CLH process and shares the same dataset as silver metal (EC 231-131-3) in the REACH dossiers, the resulting classification based on the read-across from silver ions on these two substances will be applied to all silver compounds where the ecotoxicity reference value (ERV) from silver ions has been used. Consequently, analysis of the classifications and available data has indicated that any shortcomings in the assessments of silver compounds based on read-across silver ion ERVs will be addressed as a

[14] European Commission, *Chemical Strategy for Sustainability Towards a Toxic-Free Environment*, available at https://ec.europa.eu/environment/pdf/chemicals/2020/10/Strategy.pdf

result of the CLH outcomes for EC 231-853-9 (and agreed CLH for EC 231-131-3) and no actions are currently recommended for the other substances. However, the need for a (further) group CLH on aquatic toxicity could be considered to be addressed at the same time as the CLH for reprotoxicity. This would ensure consistent obligations across all industry sectors.

The anti-microbial properties of silver and some of its compounds (resulting in uses as biocidal active substances) indicates a potential risk to microbial life beyond that targeted by biocidal uses and this is potentially reflected in a sewage treatment plant (STP) PNEC of 0.025 mg/L. The only available information to assess the hazard to microbial life in STPs is available in the biocides core dossier for silver and silver compounds (based on information from Swedish STPs, used generically) whereby a STP PEC of 0.0000305 mg/L is reported. While there are different PNECs reported in the REACH and biocides dossiers, they both indicate a very low risk quotient in STPs. Therefore based on the information available from the REACH and biocides dossiers, there does not appear to be a significant concern regarding toxicity to microorganisms in STPs and there is no need to propose any regulatory action on this aspect specifically

Based on currently available information, there is an **inconclusive** hazard for **carcinogenicity** and **mutagenicity** for silver metal, silver carbonate, all subgroup 1 and 2 silver compounds, and potassium dicyanoargentate Inconclusive hazard also applies for **skin sensitisation** for all the same substances except silver metal and for **ED** for all the same substances except silver bromide (EC 232-076-8), silver iodide (EC 232-038-0) and potassium dicyanoargentate (EC 208-047-0).

For silver metal, two non-guideline, non-GLP carcinogenicity studies, following intramuscular or intravenous injection are available in the REACH dossiers (1960, 1978). However, the relevance of these routes of exposure is questionable for human health but there seem to be local tumours at the site of injection. According to RAC (ECHA, 2022), "*no evidence of cancer in humans has been reported despite frequent therapeutic use over many years or in workers due to exposure from industrial use*", but lack of effects in humans are not considered as evidence for lack of carcinogenicity hazard in CLP. In experimental animal studies, RAC did not consider the local sarcomas induced after implantation of foils and discs of silver as relevant for classification. The REACH registrants do not self-classify for carcinogenicity due to lack of data, by any route of exposure.

The only available 2-year carcinogenicity study on silver compounds has been performed with silver zinc zeolite (EC 603-404-0, a biocide) via the oral route (in mice and rats). In the CLH proposal of silver zinc zeolite, SE CA proposed classification as Carc. 2, however RAC did not consider the effects sufficient to justify classification.

Under the BPR, a combined chronic toxicity/carcinogenicity study (OECD TG 453) has been requested for silver acetate (EC 231-853-9) to cover the data gap on chronic toxicity and carcinogenicity of soluble silver salts which have not yet been investigated. The deadline for submission of the OECD TG 453 study is in October 2024. It is suggested to wait for this study on silver nitrate before assessing this hazard further. The data to come may bring supportive information on the currently inconclusive carcinogenic properties of silver metal and the other silver compounds as identified above even if no direct read-across may be possible.

For germ cell mutagenicity, RAC concluded that the available data for silver is inconclusive due to contradictory findings and a lack of sufficient conclusive information. According to EFSA (EFSA, 2016) "*ionic silver is non-mutagenic in*

bacteria but genotoxic and clastogenic in mammalian cells in vitro [...]. No information is available on the genotoxic potential of ionic silver in vivo." Hence, the dataset on genotoxicity of ionic silver is inconclusive. As noted by RAC, silver causes testicular toxicity and some concerns remain with respect to the *in vivo* findings for both chromosomal aberrations and DNA strand breaks, potentially fulfilling the CLP criteria for germ cell mutagenicity. In addition, it must be noted that two RAC members had minority opinions in favour of classification as Muta. 2 for all metal forms of silver, highlighting a lack of full consensus on the genotoxic potential of the silver ion. Therefore, based on this assessment, there is a need to clarify the potential mutagenic properties of silver via CCH.

As for silver metal, mutagenicity is currently considered inconclusive for subgroup 1 (soluble) and 2 (poorly soluble) silver compounds as well as for silver carbonate. Both positive and negative *in vitro* studies have been reported on different silver compounds in the REACH registration dossiers, CARs and/or CLH reports. The original (unpublished or published literature) studies have not been assessed, and the applicability of read-across from the data on silver nanoparticles to some silver compounds may not be justified, in line with RAC. Therefore, data generation via CCH is proposed for silver metal, silver carbonate and all subgroup 2 substances to clarify this hazard.

For potassium dicyanoargentate (EC 208-047-0) the recent results of the *in vivo* comet assay combined with an *in vivo* mammalian erythrocyte micronucleus test with are under evaluation by ECHA (following a TPE).

For members of the group, other than silver bromide (EC 232-076-8), silver iodide (EC 232-038-0) and potassium dicyanoargentate (EC 208-047-0), the potential ED hazard properties via EAS modalities have not been assessed and therefore this hazard is inconclusive.

For the silver compounds (other than silver metal) addressed in this section the data is inconclusive for skin sensitisation. Hence, it is currently not possible to conclude on the potential skin sensitisation hazard as there is not sufficient information available. Also, for two of the silver compounds the skin sensitisation information requirement is waived due to corrosivity of the substance. Having conclusive data for skin sensitisation would be especially important for EC 208-590-3 with previously registered consumer uses as 'an active ingredient in antibiotic cream'. The need for data generation to clarify this hazard will be assessed in the **CCH** proposed for silver carbonate and all subgroup 2 substances.

Based on currently available information, for **skin sensitisation** the hazards are considered **unlikely** for **silver metal**, while for **silver methanesulphonate** (EC 219-199-2) **PB(M)T/vPvB(vM) hazards are considered unlikely**.

RAC considered that no classification for skin sensitisation is warranted for silver metal (all forms).

Although PBT/PMT is not applicable to inorganic metal compounds and elemental metals, silver methanesulphonate (EC 219-199-2) is a silver compound with organic moiety. For this substance the registrant has incorrectly indicated that the substance is inorganic. However, ECHA has checked the registration dossier for the methanesulphonate moiety as methanesulphonic acid (CAS no 75-75-2) which indicates that this moiety is not P/vP (degradation > 90% in an OECD TG 301A) leading to no concern for PB(M)T/vPvB(vM).

Currently no need to suggest (further) regulatory risk management actions for the following substances: seven substances with biocidal uses only and five NONs substances (one claimed and four unclaimed, now revoked).

The group includes seven silver compounds with biocidal uses only, without REACH registrations. Three of the substances are under evaluation by the Competent Authority (silver phosphate glass, silver borophosphate glass, silver phosphoborate glass), three are under Commission Decision of Opinion development by Biocidal Products Committee (silver zinc zeolite (Zeolite, LTA framework type, surface-modified with silver and zinc ions), silver zeolite (Zeolite, LTA framework type, ion exchanged with silver and ammonium ions) and silver copper zeolite) and for one initial application approval is in progress (silver adsorbed on silicon dioxide (as a nanomaterial in the form of a stable aggregate with primary particles in the nanoscale).

Potential for exposure and release from the biocidal uses cannot be excluded. As the substances are not registered under REACH, no information on uses is available. Therefore, the harmonised classifications and actions required under the Biocidal Product (Regulation (EU) 528/2012) sufficiently address concerns that may be caused by these substances in potential uses in biocidal the substances approved for those uses in the EU.

In case registrations under REACH will be submitted for these substances with additional uses not covered by the BPR, the need for further regulatory action may be re-considered. Also, the conclusions made in this report on other silver compounds may be considered by the BPR evaluating competent authority (eCA).

Only one of the biocidal substances, silver zinc zeolite, has harmonised classifications (Repr. 2, skin irrit. 2, Eye Dam. 1, Aquatic acute and chronic 1). The following conclusions regarding potential hazards of these substances have been made in previous work under the BPR. Human health hazard identified after RDT was concluded in the BPR assessment reports of biocides silver sodium hydrogen zirconium phosphate, silver zeolite, silver copper zeolite and silver zinc zeolite based on two studies i.e. with silver zinc zeolite and with silver sodium hydrogen zirconium phosphate. The latter study was used for reading across to the RDT of silver zeolite and silver copper zeolite which have not been tested for RDT.

No human health hazard for mutagenicity was concluded under the BPR in the assessment reports of silver sodium hydrogen zirconium phosphate, silver zeolite, silver copper zeolite and silver zinc zeolite despite the positive in vitro effects for induction of chromosomal aberrations and/or gene mutations. The conclusion under BPR was based on the negative *in vivo* Comet assay with silver zinc zeolite (List 603-404-0) used as source substance to the others not tested for in vivo genotoxicity. The conclusion is in line with the RAC Opinion for silver zinc zeolite (RAC, 2015) which concluded on no Muta classification.

No human health hazard for skin sensitisation was concluded for the same substances. RAC did not classify silver zinc zeolite for skin sensitisation in its previous opinion (ECHA, 2015). According to applicant assessment, no human health hazard for skin sensitisation was also not identified for any of the groups/types of the biocide Silver Phosphate Glass.

According to the ECHA website ED assessment is ongoing (requirement under the BPR) for several biocides (silver zinc zeolite (List 603-404-0), silver sodium zirconium hydrogenphosphate (EC 422-570-3) and silver copper zeolite (CAS 130328-19-7). ED assessment was conducted for silver zeolite (List 620-078-5)

with the conclusion that ED assessment could not be finalised as the data are considered insufficient for an assessment against the criteria laid down in Regulation (EU) No 2017/2100.

For the NONs substances limited information is available. Due to this it is not possible to clarify the potential hazards of the five NONs substances. Therefore, it is proposed that there is currently no need for EU RRM action on these substances. If the registration status changes, data generation and potentially follow up actions will be re-considered when the assessment will be revisited.

Currently not possible to suggest regulatory risk management actions for substances EC 219-641-4 (Silver docosanoate), EC 208-048-6 (Silver cyanide), EC 422-570-3 (Silver sodium zirconium hydrogenphosphate).

Based on currently available information, reproductive toxicity, carcinogenicity, STOT RE, skin sensitisation and ED hazards are considered inconclusive for silver docosanoate. Carcinogenicity and ED hazards are inconclusive for silver cyanide and silver sodium zirconium hydrogenphosphate, as well as STOT RE for the latter.

Overall the information on hazard is not sufficient to conclude on the needs for regulatory risk management actions for these substances. Data generation via CCH is proposed to clarify the inconclusive hazards, where possible and the need for RRM will be reassessed once generation of data is completed (CCH). For the other two substances registered at lower tonnage levels only actions (including data generation) will be re-considered when the assessment will be revisited if the registration status changes. Silver sodium zirconium hydrogenphosphate has also biocidal uses. The conclusions in this report made on other silver compounds may be considered by the BPR evaluating competent authority (ECA) where relevant.

Although PBT/PMT is not applicable to inorganic metal compounds and elemental metals silver docosanoate is a silver compound with an organic moiety. The docosanoate moiety has been assessed in the group of fatty acids (as EC 204-010-8) and was found to not be P/vP leading to no concern for PB(M)T/vPvB(vM).

Annex 1: Overview of classifications

Data extracted on 16 Nov 2023

EC/ List No	CAS No	Substance name	Harmonised classification	Classification in registrations
208-048-6	506-64-9	silver cyanide	-	Met. Corr. 1 H290 Acute Tox. 3 H301 Skin Irrit. 2 H315 Eye Damage 1 H318 Aquatic Acute 1 H400, M-factor: 1000.00 Aquatic Chronic 1 H410, M-factor: 100.00
208-590-3	534-16-7	silver carbonate	-	Repr. 1B H360D: May damage the unborn child. Eye Damage 1 H318 Aquatic Acute 1 H400, M-factor: 1000.00 Aquatic Chronic 1 H410, M-factor: 100.00
219-199-2	2386-52-9	silver methanesulphonate	-	Met. Corr. 1 H290 Acute Tox. 4 H302 Acute Tox. 4 H312 Skin Corr. 1C H314 Eye Damage 1 H318
219-641-4	2489-05-6	silver docosanoate	-	Aquatic Acute 1 H400, M-factor: 1000.00 Aquatic Chronic 1 H410, M-factor: 100.00
231-131-3	7440-22-4	silver	RAC opinion adopted, included in the draft ATP 22 to CLP Annex VI	Repr. 1B H360D: May damage the unborn child., specific effect: Developmental neurotoxicity Aquatic Acute 1 H400, M-factor: 1000.00 Aquatic Acute 1 H400, M-factor: 10.00 Aquatic Chronic 1 H410, M-factor: 10.00 Aquatic Chronic 1 H410, M-factor: 1000.00
231-853-9	7761-88-8	silver nitrate	Index number: 047-001-00-2, CLH ongoing. Hazard Category: Skin Corr. 1B Hazard Statement: H314 Ox. Sol. 2 Hazard Statement: H272 Aquatic Acute 1 Statement: H400 Aquatic Chronic 1 Statement: H410	Aquatic Chronic 1 H410 [intermediate (inactive)] Skin Corr. 1B H314 [intermediate (inactive)] Aquatic Acute 1 H400 [intermediate (inactive)] Repr. 1B H360D: May damage the unborn child., specific effect: Developmental neurotoxicity Oxid. Solid 2 H272 Oxid. Solid 1 H271 Met. Corr. 1 H290 Skin Corr. 1A H314 Eye Damage 1 H318 Aquatic Acute 1 H400, M-

EC/ List No	CAS No	Substance name	Harmonised classification	Classification in registrations
				factor: 1000.00 Aquatic Chronic 1 H410, M-factor: 100.00
232-033-3	7783-90-6	silver chloride	-	Repr. 1B H360D: May damage the unborn child., specific effect:Developmental neurotoxicity Met. Corr. 1 H290 Aquatic Acute 1 H400, M-factor: 1000.00 Aquatic Chronic 1 H410, M-factor: 100.00
232-038-0	7783-96-2	silver iodide	-	Repr. 1B H360D: May damage the unborn child. Aquatic Acute 1 H400, M-factor: 1000.00 Aquatic Chronic 1 H410, M-factor: 100.00
232-076-8	7785-23-1	silver bromide	-	Repr. 1B H360D: May damage the unborn child. Aquatic Acute 1 H400, M-factor: 1000.00 Aquatic Chronic 1 H410, M-factor: 100.00
233-653-7	10294-26-5	disilver(1+) sulphate	-	Repr. 1B H360D: May damage the unborn child. Eye Damage 1 H318 Aquatic Acute 1 H400, M-factor: 1000.00 Aquatic Chronic 1 H410, M-factor: 100.00
243-957-1	20667-12-3	disilver oxide	-	Repr. 1B H360D: May damage the unborn child. Repr. 2 H361f: Suspected of damaging fertility. Oxid. Solid 1 H271 Eye Damage 1 H318 Aquatic Acute 1 H400, M-factor: 100.00 Aquatic Chronic 1 H410, M-factor: 10.00
416-850-4	n/a	polyphosphoric acid, copper, sodium, magnesium, calcium, silver and zinc salt	Index number: 047-002-00-8 Aquatic Acute 1 Statement: H400 Aquatic Chronic 1 Statement: H410	-
420-090-9	n/a	GETR4	-	-
422-570-3	-	silver sodium zirconium hydrogenphosphate	Index number: 650-055-00-5 Aquatic Acute 1 Statement: H400 Aquatic Chronic 1 Statement: H410 10 M-Factor (chronic); 10 M-Factor (acute)	Aquatic Acute 1 H400, M-factor: 10.00 Aquatic Chronic 1 H410, M-factor: 10.00
428-	n/a	ARGOPHAN S	-	-

EC/ List No	CAS No	Substance name	Harmonised classification	Classification in registrations
550-0				
440-610-8	n/a	SST	-	-
460-890-5	-	[No public or meaningful name is available]	-	-
603-404-0	130328-20-0	silver zinc zeolite (Zeolite, LTA framework type, surface-modified with silver and zinc ions)	Index number: 047-003-00-3 Hazard Category: Skin Irrit. 2 Hazard Statement: H315 Hazard Category: Repr. 2 Hazard Statement: H361d Hazard Category: Eye Dam. 1 Hazard Statement: H318 Aquatic Acute 1 Statement: H400 Aquatic Chronic 1 Statement: H410 100 M-Factor (chronic); 100 M-Factor (acute)	-
620-078-5	130328-18-6	silver zeolite (Zeolite, LTA framework type, ion exchanged with silver and ammonium ions)	-	n/a (not REACH registered)
n/a	130328-19-7	silver copper zeolite	CLH intention withdrawn	n/a (not REACH registered)
608-534-1	1308069-39-8	608-534-1	-	n/a (not REACH registered)
n/a	n/a	silver borophosphate glass	-	n/a (not REACH registered)
n/a	n/a	silver phosphoborate glass	-	n/a (not REACH registered)
n/a	n/a	silver adsorbed on silicon dioxide (as a nanomaterial in the form of a stable aggregate with primary particles in the nanoscale)	-	n/a (not REACH registered)
204-786-8	126-45-4	trisilver citrate	-	-
209-254-9	563-63-3	silver acetate	-	-
220-882-2	2923-28-6	silver trifluoromethanesulphonate	-	-
222-006-4	3315-16-0	silver cyanate	-	-
232-035-4	7783-93-9	silver perchlorate	-	-
232-037-5	7783-95-1	silver (II) fluoride	-	-
232-041-7	7783-99-5	silver nitrite	-	-
232-	7784-	mercury disilver	-	-

EC/ List No	CAS No	Substance name	Harmonised classification	Classification in registrations
045-9	03-4	tetraiodide		
232-048-5	7784-08-9	trisilver arsenite	-	-
232-049-0	7784-09-0	trisilver orthophosphate	-	-
235-548-1	12271-95-3	disilver tetraborate	-	-
237-956-5	14104-20-2	silver (I) tetrafluoroborate	-	-
244-438-2	21548-73-2	disilver sulphide	-	-
247-428-6	26042-63-7	silver (I) hexafluorophosphate	-	-
607-453-9	24927-67-1	Silver(I)octanoate	-	-
677-705-0	14242-05-8	silver perchlorate	-	-
944-224-5	-	Reaction mass of titanium dioxide and silver chloride	-	-
906-230-6	-	Silver oxylate amino complex	-	Flam. Liquid 3 H226 [intermediate (inactive)] Aquatic Chronic 1 H410 [intermediate (inactive)] Eye Damage 1 H318 [intermediate (inactive)]

Annex 2: Overview of uses based on information available in registration dossiers

Data extracted on 16 Nov 2023.

EC number	208-048-6	208-590-3	219-199-2	219-641-4	231-131-3	231-853-9	232-033-3	232-038-0	232-076-8	233-653-7	243-957-1	422-570-3	428-550-0	440-610-8	460-890-5	906-230-6
REACH Annex	Annex VIII	Annex VII	Annex VII	Annex IX	Annex X	Annex IX	Annex IX	Annex VII	Annex IX	Annex VII	Annex IX	Annex VIII	<VII	<VII	Annex VII	<VII
PC 20: Products such as ph-regulators, flocculants, precipitants, neutralisation agents					F, I	F, I, **P**					I					
PC 36: Water softeners						F, I, **P**										
PC 37: Water treatment chemicals					F	F, I, **P**				F, I	F, I					
PC 2: Adsorbents					F, I, **P**	F					F					
PC 35: Washing and cleaning products						F, I										
PC 8: Biocidal products (e.g. disinfectants, pest control)					I, **P**	I, **P**				F, **P**, **A**	I					
PC 28: Perfumes, fragrances						F, I, **P**										
PC 3: Air care products						F										
PC 39: Cosmetics, personal care products		F, I, **C**														
PC 29: Pharmaceuticals		F, I, **C**			F, I, **P**					I, **A**						
PC 31: Polishes and wax blends						F, I, **P**										

PC 15: Non-metal-surface treatment products						F, I									
PC 24: Lubricants, greases, release products					F, I, **P**, **A**										
PC 25: Metal working fluids					F, I, **P**	F, I, **P**									
PC 16: Heat transfer fluids						F, I, **P**									
PC 32: Polymer preparations and compounds				**A**	F, I	F, I				F		I			
PC 1: Adhesives, sealants		I			F, I, **P**, **A**	F, I, **P**				F					
PC 9a: Coatings and paints, thinners, paint removes		I			F, I, **P**	F, I, **P**									
PC 18: Ink and toners		I			F, I, **P**	F, I, **P**	I								
PC 26: Paper and board treatment products						F, I, **P**, **A**	**P**, **C**, **A**	**P**, **C**, **A**	**A**						
PC 34: Textile dyes, and impregnating products						F, I									
PC 23: Leather treatment products					I, **P**	F, I									
PC 14: Metal surface treatment products	F, I, **P**	I	F, I		F, I, **P**, **A**	F, I				I, **A**	F, I		I		
PC 38: Welding and soldering products, flux products					F, I, **P**, **A**	F, I, **P**									
PC 7: Base metals and alloys		I			F, I, **P**, **A**	F, I									
PC 33: Semiconductors					I, **P**		I								
PC 21: Laboratory chemicals		**P**	F		F, I, **P**	F, I, **P**				I	F, I				
PC 19: Intermediate		I				I	I			I	I				I

PC42: Electrolytes for batteries					F, I,7)						F, I					
PC 30: Photo-chemicals				I		F, I, **P**, **A**	F, I	F, I	I		F					
Technical functions (all uses)	plating and metal surface treating agents	precursor, laboratory chemicals, pharmaceutical, processing aid	precursor	photochemical	precursor, plating agent, processing aid, reactive cleaning/removal agent, semiconductor and photovoltaic agent, used as base metals and alloys in welding and soldering products	precursor, laboratory chemical, photochemical	precursor, photochemical	photochemical	photochemical	precursor, pharmaceutical, plating agent, processing aid, surface treatment agent water treatment chemical	precursor					precursor

F: formulation, I: industrial use, P: professional use, C: consumer use, A: article service life; P, C and A are highlighted in red to indicate widespread use with potential for exposure/release

Annex 3: Overview of completed or ongoing regulatory risk management activities

Data extracted on 16 Nov 2023.

EC/List No	RMOA, ARN	Authorisation		Restriction *	CLH	Actions not under REACH/ CLP
		Candidate list	Annex XIV	Annex XVII	Annex VI (CLP)	
208-048-6						OEL
231-131-3					YES (ongoing)	OEL, ED, Art 95 BPR & active substance approval
231-853-9					YES	OEL, Active substance approval
232-033-3						Active substance approval
243-957-1						OEL, Active substance approval
416-850-4					YES	
422-570-3					YES	ED, active substance approval
603-404-0					YES	ED, active substance approval
620-078-5						Active substance approval
n/a, CAS 130328-19-7					YES (submitted)	ED, active substance approval
608-534-1						Active substance approval
n/a, silver borophosphate glass						Active substance approval
n/a, silver phosphoborate glass						Active substance approval
n/a, Silver adsorbed on silicon dioxide (as a nanomaterial in the form of a stable aggregate with primary particles in the nanoscale)						Active substance approval
944-224-5						Active substance approval

*Some of the broad restriction entries in the Annex XVII of REACH are not represented in the overview, e.g. when the scope of the restriction is defined by its classification or the substance identification is broad (e.g. entries 3, 28-30, 40 and 75).

There are no relevant completed or ongoing regulatory risk management activities for the other substances.